REMARKS

The Office Action has been carefully studied. No claim is allowed. Claims 5, 9, and 11-18 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 5 has been objected to for use of abbreviations. Appropriate correction is made, as supported at page 18, first paragraph, thereby obviating this objection.

New claim 18 and the amendment to claim 9 are fully supported by the specification at page 9, lines 13-18 and page 11, lines 16-21. New claims 13 and 14 are supported in the present specification at page 11, lines 22-25, and new claims 15-17 are supported at page 17, lines 21-26.

Claims 5, 9 and 11 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement in regards to leptin homologue or derivative. The examiner holds that only leptin, but not the breadth of the claims which encompasses any leptin homologue or derivative, meets the written description requirement. This rejection is respectfully traversed.

The present specification at page 11, bottom half of the page, defines "homologues" as retaining substantially similar activity to wild type leptin with preferably at least 80%, most

preferably at least 90% sequence identity to the wild type leptin sequence. The present specification at page 17, last paragraph, also defines derivatives of leptin as one or more chemical moieties attached thereto, such as water-soluble polymers, e.g., polyethylene glycol (PEG). The PEG attached to amino acid residues of leptin form pegylated derivatives of leptin.

The present specification at page 5, lines 6-8, further cites GB2292382 for disclosure of leptins and analogs thereof, such as agonists of leptins. WO96/05309, a copy of which is attached hereto, is a counterpart of GB2292382. The leptins and analogs (homologues) and derivatives thereof disclosed in WO96/05309 (GB2292382) are well known to those of skill in the art at the time the present invention was made and provides written description for the leptin homologues and derivatives recited in the present claims. WO96/05309 discloses numerous analog agonists of OB polypeptide (also termed "leptin" as defined on page 10, lines 20-21) on pages 4-6 and 37-40 as well as numerous leptin derivatives on pages 43-46. Accordingly, adequate written description of the genus is provided by the present specification in view of the knowledge in the art on leptin analogs/homologues and derivatives.

Furthermore, new claims 13 and 14, respectively, recite homologues having at least 80% and 90% sequence identity to the leptin sequence and which retain leptin activity. Thus, the

genus of homologues as well as derivatives of leptin are adequately described and satisfy the written description requirements.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 5, 9 and 11 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification, while enabling for administering leptin with or without CSC in rat, still does not reasonably provide enablement for reversibly inhibiting endothelial cell proliferation by administering leptin, a homologue or a derivative thereof in any mammal. This rejection is respectfully traversed.

The claims are now amended to delete recitation of "reversible" inhibition and are directed to inhibition of angiogenesis. Attached hereto is a publication, Cohen et al., *J. Biol. Chem.* 276:7697-7700 (2001), for the examiner's consideration. This Cohen et al. paper, authored by the present inventors and their co-workers, was published after the filing of the present application and clearly supports leptin's angiostatic effect in adipose tissue of ob/ob mice *in vivo* by inducing expression of Ang-2 and thereby causing blood vessel regression. The paper concludes that leptin provides a strong angiostatic rather than angiogenic single (page 7699, right column, first

paragraph of the discussion section). Accordingly, the presently claimed method is indeed enabling to those of skill in the art.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /ACY/
Allen C. Yun
Registration No. 37,971

ACY:pp
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
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